

per day up to a maximum dose of 3.0 mg per day, by subcutaneous injection. Adverse effects include nausea and vomiting, and among patients with a family history of multiple endocrine neoplasia, a slightly increased risk of medullary thyroid cancer.⁷¹⁰ Liraglutide is FDA approved for long-term treatment of obesity (with or without T2DM) in children 12 years and older.

Melanocortin 4 receptor (MC4R) agonists, such as setmelanotide, act on the MC4R pathway to restore normal function for appetite regulation that has been disrupted because of genetic deficits upstream of the MC4 receptor. MC4 receptors in the brain regulate hunger, satiety, and energy expenditure. The daily dose is 1 to 3 mg daily, given subcutaneously, and results in weight loss of 12% to 25% over 1 year in a small, uncontrolled study of patients with these rare deficits. Common adverse effects include injection site reaction and nausea. Setmelanotide is FDA approved for patients 6 years and older with proopiomelanocortin (POMC) deficiency, proprotein subtilisin or kexin type 1 deficiency, and leptin receptor deficiency confirmed by genetic testing.

Phentermine is a central norepinephrine uptake inhibitor but also nonselectively inhibits serotonin and dopamine reuptake and reduces appetite. Recommended doses include 7.5 mg, 15 mg, 30 mg, or 37.5 mg, and adverse effects include elevated BP, dizziness, headache, tremor, dry mouth, and stomachache. Adverse effects are dose-dependent; however, effectiveness does not always increase with increasing dose. Phentermine is FDA approved for short-course therapy (3 months) for adolescents 16 years or older.

Topiramate is a carbonic anhydrase inhibitor and suppresses appetite

centrally through largely unknown mechanisms. The major adverse effect is cognitive slowing, which can interfere with academic concentration or other activities of daily living. In addition, topiramate is a potential teratogen and requires counseling and reliable birth control for patients able to become pregnant. Typical dosing for headache prevention ranges from 25 mg a day to 100 mg a day in twice daily doses. Although topiramate has an indication for treatment of binge eating disorder in adults (age ≥ 18), only 1 study has evaluated the use of topiramate in children, and it did not differ from placebo. Topiramate is currently FDA approved for children 2 years and older with epilepsy and for headache prevention in children 12 years and older.

Phentermine and topiramate as a combination medication is approved for weight loss in adults. Recent data show that among adolescents 12 to 17 years of age with documented history of failure to lose sufficient weight or failure to maintain weight loss in a lifestyle modification program (mean age, 14 years; mean BMI, 37.8 kg/m²), BMI percent change at 56 weeks was -10.44 (high dose; 15 mg/92 mg) and -8.11 (mid dose; 7.5 mg/46 mg) as compared with placebo.⁷³¹ Treatment also improved HDL and TG cholesterol profiles. Adverse events reported were not more common than placebo in the high- or mid-dose range.

Lisdexamfetamine is similar in mechanism to phentermine and is a stimulant-class medication approved for children 6 years and older with ADHD. It has an indication for treatment of binge eating disorder in patients 18 years and older; thus, it is used off-label for children with obesity. However, no evidence is available at the time of this review

to demonstrate safety or efficacy for the indication of obesity in children.

Prescriber Qualifications

Weight loss medications require the same oversight and expertise in management as other medications used in pediatric care. To adequately inform patients and parents about the risks and benefits of off-label or experimental use of new therapies, pediatricians and other PHCPs who prescribe weight loss medications should have knowledge of the patient selection criteria, medication efficacy, adverse effects, and follow-up monitoring guidelines. In addition, injectable medications may require additional teaching for families that is not available in all primary care offices. Pediatricians and other PHCPs may choose to refer to pediatric obesity experts or treatment centers for prescribing weight loss medication.

No current evidence supports weight loss medication use as a monotherapy; thus, pediatricians and other PHCPs who prescribe weight loss medication to children should provide or refer to intensive behavioral interventions for patients and families as an adjunct to medication therapy.

J. Pediatric Metabolic and Bariatric Surgery

It is widely accepted that the most severe forms of pediatric obesity (ie, $\geq$ class 2 obesity; BMI ≥ 35 kg/m², or 120% of the 95th percentile for age and sex, whichever is lower) represent an “epidemic within an epidemic.” Moreover, severe obesity is a harbinger of the establishment and cumulative progression of numerous related comorbidities, diminished long-term health status, and shortened life expectancy.^{654,739}

For adults, the evidence supporting the clinical indications and associated recommendations on the use of metabolic and bariatric